REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

1. Claim Amendments

The claims have been amended to encompass enhancing transduction efficiency for an expression vector encoding a phospholamban mutant by placing the patient in a state of hypothermia (claim 70). Under dependent claims, the patient may also be suffering from other conditions at the time of treatment and/or receive co-administered SERCA-2.

No new matter is added to the claims or the application by these amendments. Claims claims 1-45, 52-55, 57-58, 61-69 and 73-76 are presently cancelled, while claims 46-51, 56 and 59-60 were previously cancelled. Claims 77 and 79-85 are as previously presented. Claims 70-72, 78 and 86 are amended. The amended claims, as well as newly added claims 87-97, are based on subject matter that was either recited in the claims as originally presented and/or present in the disclosure as filed. In addition, typographical errors in the claims have been corrected; for example, the expression vector referred to in Claim 77 as "adenovirus associated viral vector" is correctly referred to as "adeno-associated viral vector," and the claim has been amended accordingly.

Entry of the proposed amendments is respectfully requested.

2. Response to Rejection of Claims 80-82 and 84-85 Under 35 USC Section 112, First Paragraph (Written Description).

The claims are objected to for lack of written description as to gene therapy performed in the heart with any phospholamban molecule. Without prejudice to later prosecution of broader claims, Applicant has amended the claims to be directed to the embodiment exemplified in Example 2 of the application, for enhancing the transduction efficiency of a gene therapy vector (in particular, one encoding a phospholamban molecule). It is respectfully submitted therefore that the rejection as stated is moot in view of the amendments made herein.

In lieu of the rejected claims, amended and newly added claims 70-72 and 77-91 are now directed to means to enhance the efficacy of gene therapy for cardiomyopathies by increasing the transduction efficiency of an expression vector for encoding a therapeutic molecule; in particular, a mutated phospholamban molecule. To this end, the treated patient is placed into a state of hypothermia.

The hamster animal model whose use exemplifies the practice of the invention (see, Example 2, paragraphs 0032-0034) is accepted in the art as displaying phenotypic features of human primary dilated cardiomyopathy phenotypic features of human primary dilated cardiomyopathy (see, specification at paragraph 0010). As demonstrated, placing the animals in a state of deep or mild hypothermia increased the efficiency with which a viral expression vector was introduced into cardiac muscle cells by as much as 77% (paragraph 0034). For use in humans, the technique of placing a patient undergoing heart surgery into a state of hypothermia is art accepted (see, specification at paragraph 0027).

The method may be utilized with any gene (see, e.g., paragraphs 0030 and 0031, re experimental use of the beta.-galactosidase gene with a nuclear localization signal sequence (Ad.CMV LacZ), the hamster .delta.-sarcoglycan gene (Ad.CMV .delta.-sarcoglycan) driven by the CMV promoter, and an AAV S16E phospholamban gene). However, for purposes of compact prosecution, the claims as amended are directed to delivery of a phospholamban molecule, without prejudice to later prosecution of broader claims. Thus, the invention as claimed is fully supported by the present disclosure.

Reconsideration of amended claims 70-72 and 77-86, and favorable consideration of newly added claims 87-91, is respectfully requested.

2. Response to Rejection of Claims 1-4, 6-22, 31, 52-55, 57-58 and 61-86 Under 35 USC Section 112, First Paragraph (Enablement).

Claims 1-4, 6-22, 31, 52-55, 57-58 and 61-86 are rejected as not being enabled by the Specification. In particular, the Office Action suggests that while a method for gene therapy of cardiac conditions with a S16E phospholamban mutant is enabled, use of any other molecules in the invention is not. In view of the cancellation of claims 1-4, 6-22, 31, 52-55, 57-58 and 61-69, the rejection as to those claims is moot. With respect to claims 70-86, and newly added claims 92-97, all to methods of gene therapy, the claims are now directed to gene therapy of cardiac disease using a particular phospholamban molecule; i.e., one with a S16E mutation to cardiac muscle. The amendments to claims 70-86 is made without prejudice to later prosecution of broader claims.

According to the Office Action, claims to gene therapy of cardiac conditions with the S16E molecule are enabled by the present disclosure. Applicant submits that the same conclusion should be reached with respect to the amended and newly added claims. In particular, as demonstrated by the hamster model data provided in Examples 6 through 8 (paragraphs 0039 through 0043), administration of the S16E increases cardiac contractility and reduces cardiomyopathy-related damage to the heart muscle. These data provide direct evidence that PLB inhibition can lead to chronic reversal of heart failure by employing a novel AAV mediated gene therapy strategy, even at stages of the disease that correspond to severe near end-stage human heart failure (late NYHA Class III).

Applicant therefore submits that the invention of amended claims 70-86 and newly added claims 92-97, as acknowledged in the Office Action, is fully enabled by the present disclosure.

Reconsideration of the amended claims, and favorable consideration of the newly added claims, is respectfully requested.

3. Response to Objection to Claims 7 and 44 Under 35 USC Section 112, Second Paragraph.

Claims 7 and 44 are objected to for lack of antecedent basis, but the objections are rendered moot by the cancellation of both claims.

CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872.

If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

Respectfully submitted,

Date November 14, 2005

By

FOLEY & LARDNER LLP
Customer Number: 30542
Telephone: (858) 847-6720
Facsimile: (858) 792-6773

Stacy L. Taylor
Attorney for Applicant
Registration No. 34,842